

THE
CALABAR BEAN

AS
A NEW AGENT IN OPHTHALMIC MEDICINE.

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AS A NEW OPHTHALMIC AGENT.

FOR more than a year past I have recognised the numerous advantages that would flow from the discovery of a substance which, when applied to the conjunctiva, should produce effects exactly opposite to those well known to result from belladonna or atropine; which should stimulate the muscle of accommodation and the sphincter pupillæ as the above-named remedies paralyze them. With the view of discovering such an agent, I endeavoured to ascertain from experiments of my own, and from the writings of previous observers, whether any of the common vegetable principles possessed this property. These investigations were, however, productive of no satisfactory results, until my friend Dr Fraser informed me that he had seen contraction of the pupil result from the local application of an extract of the ordeal bean of Calabar. I resolved to investigate the action of this substance, and, above all, to ascertain whether it exerted any influence on the accommodation of the eye. With some difficulty I got a few Calabar beans, and, with the view of obtaining their active principles in a convenient form, prepared from them three extracts of varying strengths in the following manner:—The weakest of the three was made by thoroughly digesting gr. xxx. of the powdered Calabar bean in alcohol, carefully evaporating the strained fluid to dryness, and then adding to the residue ʒj. of water. This formed a muddy solution of a light reddish brown tint. In strength, one minim of this solution corresponded to about half a grain of the bean. The second extract was formed by evaporating a portion of the first to about a quarter of its volume; so that one minim of this extract corresponded to about two grains of the bean. The third extract was the strongest, and was prepared like the first, except that the proportions differed; so that one minim of it in strength corresponded to four grains of the bean.

With these solutions, I then proceeded to perform the following experiments,—in which I had the able assistance of Dr Grainger Stewart,—with the intention of elucidating the exact effects the Calabar bean is capable of producing on the eye:—

Experiment 1.—On the 17th of January, I carefully examined the condition of my eyes, and found that with both my sight was normal. I could see distant objects perfectly distinctly, and could read the finest print (No. 1 of Jaeger), at five inches distance, with either eye. Each pupil measured two lines in diameter, and acted readily under the influence of light. These points having been

determined, I introduced a drop of the weakest extract of the Calabar bean into my left eye, at 10 minutes past 12 o'clock. Its introduction occasioned no further irritation than a drop of simple water would produce.

No change was observed in the condition of the eyes until ten minutes thereafter, when, upon looking with the left eye, all objects beyond the distance of about a foot appeared dim and indistinct, but within that distance clear and well defined; while objects at all distances appeared nearer and larger than natural. Vision in the right eye remained unaltered. No difference was visible in the size of either of the pupils. A feeling of straining and heaviness was felt in the left eye similar to that experienced after a prolonged inspection of fine objects near the eye.

At 12.30, or 20 minutes after the introduction of the extract, a marked alteration in the size of the pupils was observable; the left pupil being only 1 line in diameter, while the right measured fully two lines. Looking with the left eye, all objects beyond nine inches from the eye appeared very dim, and at all distances everything seemed about a half larger than natural, and nearer to the eye. Vision in the right eye was unaffected.

At 12.40, the left pupil measured only $\frac{2}{3}$ of a line, while that of the right eye had dilated to $2\frac{1}{2}$ lines. The furthest point of distinct vision with the left eye was 8 inches from the eye. In other respects no alteration was observable since last report.

At 1.20, the pupils measured on the left side $\frac{1}{2}$ a line, on the right 2 lines. With the left eye objects could with some effort be seen distinctly to the distance of about 10 yards, but, as before, larger and darker than with the other eye. When reading with both eyes, a sensation of heaviness and fatigue was soon felt in the left. Vision in the right eye continued unaltered.

At 6 o'clock, the left pupil had dilated to 1 line, while the right had contracted to $1\frac{3}{4}$ line. Vision with the left was somewhat improved, and with an effort distant objects could be distinctly seen. Both pupils contracted under the influence of light, both singly and sympathetically. At 12 o'clock, the left pupil measured $1\frac{1}{2}$ line, the right $2\frac{1}{2}$ lines, and the same symptoms were present as at last report, only to a less marked degree. A dull aching and heaviness was experienced in the left eye consequent upon its exercise in reading and writing.

On the following morning, there was still an appreciable difference in the size of the pupils, and vision with the left eye was still slightly affected; but the symptoms gradually subsided, and in the afternoon completely disappeared.

The results obtained from this experiment were, that the Calabar bean acted first on the accommodation of the eye, causing indistinct vision of distant objects to such an extent that all objects beyond 8 inches from the eye appeared dim and indistinct. The next marked effect produced was contraction of the pupil, its diameter being reduced from 2 lines to $\frac{1}{2}$ a line. As a natural consequence

of less light passing to the retina of the eye experimented on, the pupil of the other eye became sympathetically somewhat dilated, while with the affected eye all objects appeared darker than natural. It is interesting to observe, that while the affection of the accommodation of the eye is the symptom first developed, it also is the first to subside, for we find that while the contraction of the pupil is at its maximum at 1.20, the affection of vision had already decidedly diminished. From the very small size of the pupil, it was very difficult to ascertain whether it acted under the influence of light or not. On the occasion of one of the reports (where it is mentioned), it was distinctly observed to do so.

Experiment 2.—Having ascertained that my eyes had returned to their normal condition, and that each pupil, as before, measured 2 lines, and acted under the influence of light, I again, on January 20th, introduced a drop of the weakest extract of the Calabar bean into my left eye at 8.30 A.M.

At 8.40 the pupils were unaffected. With the left eye objects beyond 9 inches appeared dim, enlarged, and nearer than with the other eye, and a concave glass, of 10 inches negative focus, was required to enable me to see distant objects distinctly. With this concave glass the nearest point at which I could see objects distinctly was 9 inches from the eye.

At 9.5 the left pupil measured $\frac{3}{4}$ of a line, the right 2 lines. To see distant objects clearly with the left eye, a concave glass of 8 inches negative focus was now required, and with this glass the "near-point" of distinct vision was 5 inches from the eye. Both pupils acted under the influence of light. Vision in the right eye was unaffected.

A drop of a solution of atropine (gr.ij to $\bar{3}$ i) was now introduced into the left eye.

At 9.30, the left pupil had sensibly increased in size, and measured 1 line, while the right measured $1\frac{1}{4}$ line. A concave glass of 12 inches negative focus was now sufficient for distinct vision of distant objects with the left eye.

At 10, the left pupil had become dilated to 3 lines, the right pupil remaining unaffected. With the left eye objects beyond 3 feet could alone be distinctly viewed, and all objects appeared smaller and more distant than natural. The left pupil was insensible to the influence of light. A drop of the extract of Calabar bean, of medium strength, was introduced into the left eye.

At 10.30, all objects beyond 8 inches were clearly seen with the left eye, and the pupils measured 3 lines on the right side and $1\frac{3}{4}$ line on the left.

A quarter of an hour later, the "near-point" of distinct vision had receded to 12 inches from the eye, but the pupils had undergone no alteration in size.

Another drop of the same extract of the Calabar bean, as was last employed, was again applied to the left eye.

At 11.30, vision with the left eye was perfectly distinct beyond 9

inches from the eye. There was no alteration in the size of the pupils.

At 1.30, all objects within 12 inches appeared dim and indistinct with the left eye, while everything beyond that distance was clear and well-defined. The left pupil was $2\frac{3}{4}$ lines in diameter, the right $1\frac{1}{2}$ line.

Another drop of the extract of the Calabar bean was introduced, which, as before, improved the condition of the accommodation of the eye, the effects lasting about four hours. The application of the Calabar bean was repeated other three times, the effects at each successive application being more marked, and enduring longer. In two or three days, the effects of the atropine and Calabar bean disappeared.

This experiment led me to the conclusion that the Calabar bean and belladonna are exactly antagonistic in their action on the eye; and I ascribed the temporary nature of the improvement effected by the Calabar bean on the eye under the influence of atropine, to the fact that the atropine solution was much stronger than the extract of the Calabar bean I had employed. To put this to the proof I performed the following experiment:—

Experiment 3.—On February 2d, at 2.10 p.m., I introduced into each of my eyes a drop of a solution of atropine of the strength of gr.ss to 3i. By examination, prior to the introduction of the drops, I had ascertained that vision in both was normal—all objects beyond 5 inches from the eye being distinctly perceived—and that the left pupil measured 2 lines, and the right fully $1\frac{3}{4}$ line in diameter.

At 3.20, the physiological effects of the atropine had manifested themselves pretty decidedly. The right pupil was $3\frac{3}{4}$ lines, the left $3\frac{1}{2}$ lines in diameter; the nearest point of distinct vision was—left eye, 8 inches; right eye, 12 inches.

A drop of the strongest extract of the Calabar bean was now introduced into my right eye.

At 3.40, the pupils measured $3\frac{1}{2}$ lines each. In vision there was a marked difference between the eyes, for with the right I could read only very large type (No. 18 of Jaeger, “Canon” type) at 2 feet distance; while with the left, at that distance I could read moderate-sized print (No. 8 of Jaeger, “Small Pica” type).

At 3.55, the state of vision in my right eye was very peculiar. I could only see objects distinctly between $6\frac{1}{2}$ inches and 9 inches from the eye; anything nearer to the eye than $6\frac{1}{2}$ inches, or further from it than 9 inches, appearing misty and dim. With the left eye everything appeared distinct beyond 12 inches. The right pupil measured 3 lines, the left $3\frac{1}{2}$ lines in diameter.

At 4.15, the extent of clear vision with the right eye had very much increased—being in fact almost normal—all objects beyond 6 inches being seen with perfect distinctness. The nearest point of distinct vision in the left eye was 15 inches. There was no alteration in the size of the pupils from last report. Looking with the right eye objects appeared much larger than when viewed with the

left. With the right eye I was able to read small print without the slightest inconvenience, while with the left I was unable to read any but large-sized print, and that only when held at a considerable distance from the eye.

At 6.55, the effects of the Calabar bean were passing off the nearest point of clear vision in the right eye, being about 18 inches from the eye. Another drop of the strongest extract of the Calabar bean applied to right eye.

At 7.5, distinct vision with the right eye ranged from 6 to 9 inches from the eye; at 7.15 it ranged between $5\frac{1}{2}$ inches and 8 inches; at 7.55 between 5 inches and 15 inches; and at 8.15, objects at all distances beyond 5 inches could be most clearly defined. Very little alteration was observed in the size of the pupils or the vision of the left eye. No further application of the Calabar bean was made to the right eye, as the effects of the last application lasted until the effects of the atropine had almost passed off, and exhibited a marked contrast to the left eye, in which the atropine acted uncontrolled.

I have narrated these experiments somewhat in detail, so as to elucidate, as far as possible, the method of action of this new agent and its energy. These experiments prove that the local application of the Calabar bean to the eye induces,—*first*, A condition of short-sightedness. That this is present, and the cause of the indistinctness of distant vision cannot be doubted, as it is relieved by the use of concave glasses. The fact that objects appear larger and nearer than natural may be attributed to the induced myopia. And, *second*, It occasions contraction of the pupil, and sympathetically dilatation of the pupil of the other eye. We further observe that atropine possesses the power of counteracting its effects, and, *vice versa*, that it is capable of overcoming the effects produced by atropine. The first symptom noticed is dimness of distant vision, and shortly after the pupil becomes contracted; the symptoms also subside in the same order, first the derangement of accommodation, and then the affection of the pupil.

Let me now say a few words as to the method of action of the Calabar bean. In respect to its effects on the pupil they might be produced either by causing contraction of the circular fibres of the iris, or by paralyzing its radiating fibres. I am inclined to believe that the contraction of the pupil is due to increased action of the sphincter pupillæ, and this chiefly on the ground that the other effects produced by the Calabar bean can only be explained by an induced contraction of the ciliary muscle—the muscle of accommodation; and as the sphincter pupillæ and ciliary muscle are both supplied by the ciliary nerves, I think the most feasible explanation of the action of the Calabar bean on the eye is to regard it as a stimulant to the ciliary nerves. In favour of this view we have the feeling of straining in the eye shortly after the physiological effects are produced. The alteration, too, in the accommodation of the eye exhibits much of the character of a spasmodic action; thus

we find in experiment *third*, after the second application of the Calabar bean, that the extent of distinct vision is limited to 3 inches, viz., from 6 to 9 inches from the eye, but an hour after distinct vision extends to any distance beyond 5 inches. It has also been observed that the accommodation of the eye is not usually affected in cases where contraction of the pupil is due to lesion of the sympathetic (exemplified in a case narrated by Dr von Willebrand in the *Archiv für Ophthalmologie*, vol. i., where contraction of the pupil depended on the pressure of enlarged glands on the cervical sympathetic, and where no affection of the accommodation was present).

As regards the cases in which this substance may be applied in practice, it is applicable in all instances where atropine is used to render the examination of the eye more perfect or more simple. This includes two classes of cases, those in which dilatation of the pupil is either necessary or desirable to aid ophthalmoscopic examination, and those in which paralysis of the ciliary muscle is necessary, in order to ascertain the state of the accommodation of the eye.

In cases of retinitis, with photophobia, I think it might be advantageously employed to diminish by contraction of the pupil the access of light to the retina, and this more especially in those cases of this disease where the pupil has been dilated for the purpose of ophthalmic examination.

The cases, however, in which I should expect this remedy to produce the most beneficial effects are those in which paralysis of the ciliary muscle occurs as a consequence of long-continued debilitating disease. Cases of this kind are occasionally reported as following attacks of typhus or other fevers. The dimness of vision that forms a frequent sequela of diphtheria appears also to be due to this cause, judging from the symptoms detailed by Dr Begbie in an admirable paper on diphtheria, recently published in this Journal; therefore, in these cases, good effects may be expected from the use of the Calabar bean.

In cases of ulceration at the margin of the cornea, leading to perforation, or even when prolapsus of the iris has just occurred, as well as in cases where the iris has a tendency to protrude through a corneal wound, the contraction of the pupil induced by this agent might prove serviceable by drawing the iris away from the circumference.

I have shortly pointed out the cases in which I consider this remedy may prove useful, but have as yet had but little opportunity to test it practically; I think, however, there can be little doubt that in the Calabar bean we possess an agent that will soon rank as one of the most valuable in the ophthalmic pharmacopœia.

